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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/516,950	08/11/2005	Christopher J. Speirs	SPEI3002	1941

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EXAMINER	
TRAN, SUSAN T	

ART UNIT	PAPER NUMBER
1615	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/516,950	SPEIRS ET AL.	
	Examiner	Art Unit	
	S. Tran	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 April 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *43-62* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *43-62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *04/07/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Objections

Claim 62 is objected to because of the following informalities:

Line 8 of the claim recites "the surface of second the pellet", which should read "the surface of the second pellet". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 43-62 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. It appears that the present specification does not provide support for the limitations "wherein said coating material is applied directly onto the surface of the pellets", and "wherein the pH dissolution dependent coating material is contiguous with the surface of the first/[second] pellet".

Claim Rejections - 35 USC § 102

> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 43-49, 55, 57 and 62 are rejected under 35 U.S.C. 102(e) as being anticipated by Fischer et al. US 6,267,990.

Fischer teaches a controlled release preparation comprising at least two populations of pellets: a first delayed release type of pellet; and a second delayed release type of pellet (abstract; claims). The ratio of the first and second delayed release type of pellet ranges from 1:2 to 1:7 (column 2, lines 10-14). The pellets of the first and second delayed release can be coated with the same materials, such as Eudragit or Aquacoat (column 2, lines 39-62).

Claims 43-53, 55, 58, 59 and 62 are rejected under 35 U.S.C. 102(b) as being anticipated by Heinicke et al. US 5,834,024.

Heinicke teaches a controlled release formulation comprising short and long lag pellets of diltiazem (abstract). The diltiazem core is coated with polymer or mixture of polymers such as Eudragit S, Eudragit L, or Eudragit L 30D (column 5, lines 24-44). The thickness of the coating is increasing or decreasing to obtain the desired short and long lag pellets (column 4, lines 21-38). Example 1 shows the short lag pellet

comprises about 12% weight gained of the coating polymer, and the long lag pellet comprises about 29% weight gained of the coating polymer. Heinicke further teaches the particle size of the pellet is about 1400 µm (example 1). The combined pellets are filled into capsule (column 6, line 64).

Claim Rejections - 35 USC § 103

Claims 43-53, 55-59 and 62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Heinicke et al. US 5,834,024.

Heinicke is relied upon for the reason stated above. Heinicke further does not teach the claimed ratio of the short and long lag pellets. However, it would have been obvious to one of ordinary skill in the art to, by routine experimentation determine a suitable coating weight gain, as well as the ration between the short and long lags depends in the release profile desired. This is because Heinicke teaches a controlled release dosage form effective to permit release of active agent at different cites in the GI tract over a 24 hours period, and because Heinicke teaches a weight gain of about 29%, with a mixture of 40% short lag and 60% long lag pellets (example 1).

Claims 43-62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Speirs US 5,834,021, in view of Andre et al. EP 1064938 A1.

Speirs teaches a controlled release dosage form comprising enterically coated pellet of prednisolone metasulphobenzoate incorporated into enterically coated capsule (abstract; and column 5, lines 61-67). Enteric coating polymer includes Eudragit S or

Eudragit L (column 5, lines 9-34). The pellet has a diameter in the range of 700-1700 μm (column 4, lines 66-67). Spear further teaches that the thickness of the Eudragit coating on the pellets is between 15-30% based on the uncoated granule (column 5, lines 39-52).

Speirs does not expressly teach dosage form comprising plurality of particle with different release profiles.

Andre teaches a multiparticulate dosage form comprising active core, coating with film forming polymer such as Eudragit polymer (abstract; and paragraphs 0015-0017). Andre also teaches capsule comprising different population of coated multiparticulate dosage form with different release profiles (page 5, lines 38-43; and examples). Active agent includes prednisolone (paragraph 0024). Thus, it would have been obvious to one of ordinary skill in the art to modify the prednisolone dosage form of Speirs to prepare a dosage form with at least a timed pulse in view of the teachings of Andre. This is because Andre teaches that a timed pulse release dosage form allows targeting of a drug to a given site of the GI tract, in particular the colon (paragraph 0006), because Andre teaches a pulsed release dosage form that allows reduced dosing frequency, because Andre teaches a pulsed release dosage form suitable for drugs including prednisolone, and because Speirs teaches the desirability to include a plurality of the coated pellets in a capsule for the delivery of prednisolone to the intestine (column 4, lines 38-43).

Response to Arguments

Applicant's arguments filed 04/07/09 have been fully considered but they are not persuasive.

Applicant argues that Heinicke *et al* exemplifies a mixture of short and long lag pellets wherein each pellet consists of sugar spheres coated with a diltiazem coating to form the cores which are then divided into two parts, the first part being coating with a mixture of Eudragit RS and Eudragit RL and the second part being coated with a thicker coating of the same coating formulation. However, there is no disclosure in Heinicke *et al* of coating the surface of pellets directly with a pH sensitive material as a film forming material for pH-mediated release of an active agent. This recitation is recited in each of independent Claims 43, 61, and 62. The remaining claims at issue are also novel over Heinicke *et al* by virtue of the dependency of these claims from new Claim 43, 61, and 62.

However, applicant's attention is called to column 5, lines 25-45, for the teaching of coating layer may alternatively be comprised of pH sensitive materials such as Eudragit S, Eudragit L, and Eudragit RL. Accordingly, the rejections by Heinicke is maintained.

Applicant argues that neither Speirs nor Andre *et al* provides any suggestion that would prompt the skilled person to consider coating different pluralities of uncoated pellets with different thicknesses of a pH sensitive coating material for pH controlled release of an active. Furthermore, neither of these documents provides any suggestion that a composition comprising different pluralities of pellets coated in this way would

have any effect on the rate of release of the active relative to pH, let alone increasing the release rate as the pH of the surrounding medium increases.

However, in response to applicant's argument that *neither Speirs nor Andre et al provides any suggestion that would prompt the skilled person to consider coating different pluralities of uncoated pellets with different thicknesses of a pH sensitive coating material for pH controlled release of an active*, applicant's attention is called to Speirs at column 5, lines 39-52, for the teachings that thickness of coating required on the pellets will depend upon the dissolution profile of the particular coating materials and possibly also upon the dissolution profile of any enteric coating on the dosage fork. Thus, one of ordinary skill in the art would have been motivated to, by routine experimentation optimize the thickness of each pellet population depends upon the release profiles desired given the teachings of Speirs in view of Andre to obtain the claimed invention.

Moreover, in response to applicant's arguments, the burden is shifted to applicant to show that the coating comprising Eudragit L or Eudragit S in Speirs does not exhibit the claimed property, namely, increasing the release rate as the pH of the surrounding medium increases. This is because Speirs teaches coating polymers that is insoluble in gastric juice and in intestinal fluid below pH 7 but is soluble in lower intestinal fluid (column 5, lines 14-16), and because both of the Eudragits L and S are used by the applicant as a pH sensitive materials (see specification at pages 13-14).

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to S. Tran whose telephone number is (571) 272-0606. The examiner can normally be reached on M-F 8:00 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. Tran/
Primary Examiner, Art Unit 1615